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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,269	MORISHITA ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-52 and 55-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-52 and 55-85* is/are rejected.

7)☒ Claim(s) *50, 55, 60, 71* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/9/2006* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/06; 10/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Examiner acknowledges the election, without traverse, of Group IV directed to a method of treating a disease of the respiratory system, in the reply filed on 25 October 2007.

Claim Status

Claims 45-52 and 55-85 are pending. Claims 1-44 and 53-54 are cancelled. Claims 55-85 are newly added. Claims 45-52 and 55-85 are under current examination.

Sequence Compliance

Sequence Listing and CRF have been received and are acknowledged by examiner. A statement that the Computer Readable Form (CRF) and the Sequence Listing are identical has been submitted and is acknowledged by examiner.

Oath/Declaration

The new oath or declaration, having the signatures of all inventors, received on 22 December 2006 is in compliance with 37 CFR 1.63.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 9 January 2006 and 25 October 2007 consisting of 13 sheets are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims benefit as a 371 of PCT/JP04/09838 (filed 07/09/2004). The application also claims benefit from foreign application PCT/JP2003/08740 (filed 07/09/2003). The instant application has been granted the benefit date, 9 July 2003, from PCT/JP2003/08740.

Claim Objections

Claim 50 is objected to because of the following informalities: Claim 50 contains the word, "Into" in the middle of the sentence. In correct grammatical form, the word, "into" should not be capitalized. Appropriate correction is required.

Claims 55 and 60 are objected to because of the following informalities: Claim 55 contains the word, "NP-kB." The examiner believes this to be a typographical error, referring to "NF-kB" and will examine the claim as if it refers to "NF-kB." Appropriate correction is required.

Claim 55 is also objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s)

in proper dependent form, or rewrite the claim(s) in independent form. Claim 55 is actually broader than claim 45, since it encompasses more than merely the "decoys" of claim 45, but also encompasses fragments, variants, and derivatives of the decoys.

Claim 71 is objected to because of the following informalities: Claims 71 uses the nomenclature "0,1" which is not standard US manner of referring to decimals. The examiner requests that the more common US method of referring to decimals, "0.1" be substituted for this term.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

WRITTEN DESCRIPTION

Claims 45-52 and 55-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the

application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 USC § 112, p 1 "Written Description" Requirement;* (Federal Register/Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Claim 45 is broadly drawn, such that it applies to a method for treating and/or preventing a disease of the respiratory system comprising administering a genus of NK-kB decoys. However, the working examples provided in the instant application only demonstrate individual species of NF-kB decoys, specifically SEQ ID NO:1 and 3. In addition, claim 59 is directed to variants, fragments, and derivatives of a NF-kB decoy.

The specification states, "[t]he term 'decoy' or 'decoy compound' refers to a compound which binds to a site on a chromosome to which NF-kB bind to [*sic*], or a site on a chromosome (hereinafter referred to as a target binding site), to which another transcription regulatory factor for a gene controlled by NF-kB binds to, and antagonizes the binding of NF-kB to target binding sites thereof. Representatively, the decoy or the decoy compound includes a nucleic acid and analogs thereof" (pages 23-24). Additionally, the specification indicates a "NF-kB decoy is a decoy set forth in SEQ ID NO:1" (page 13, lines 32-33). Still further, the specification indicates that modifications, mutants or variants of SEQ ID NO:1 can be examples of decoys (page 24, lines 19-35)

and specifically identifies SEQ ID NO:3 was such a variant (page 25, line 9). The working examples (pages 58-72) demonstrate administration of decoy oligonucleotides, SEQ ID NO:1 and 3 in rat models of asthma, rat models of rhinitis, and dog models of COPD.

Essentially, the applicant has described the NF-kB decoys in functional language, and has only a few examples of antisense oligonucleotides which satisfy the definition of NF-kB decoys. However, the term "decoy" as described above, could easily encompass a large genus of proteins, with transcription factor binding motifs capable of binding the NF-kB binding sites, but which are competitors of NF-kB. The specification gives no guidance for this type of decoy. Furthermore, besides these three oligonucleotides (SEQ ID NO:1 and 3), the specification does not provide any guidance for other oligonucleotides which might satisfy the functional definition provided in the specification, "a compound which binds to a site on a chromosome to which NF-kB binds." In addition, claim 59 is directed to variants, fragments, and derivatives of a NF-kB decoy which "has a biological activity". This is clearly functional language and no corresponding structural limitations which provide a "biological activity" by these fragments, variants, and derivatives are taught by the specification.

See MPEP § 2163, which states "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, ***even when accompanied by a method of obtaining the claimed sequence."***

The Revised Interim Guideline for Examination of Patent Applications under 35 USC § 112, p1 "Written Description" Requirement (Federal Register/ Vol 66. No 4, Friday January 5, 2001) states "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (column 2, page 71436, emphasis added).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE SOUGHT, HE OR SHE WAS IN POSSESSION OF THE INVENTION. THE INVENTION IS, FOR PURPOSES OF THE 'WRITTEN DESCRIPTION' INQUIRY, *WHATEVER IS NOW CLAIMED.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize the [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Given the breadth of the instant claims and the functional language with which the term, "NF-kB decoy" has been described (see above), and the lack of examples

which utilize NF-kB decoys other than SEQ ID NO:1 and 3, the examiner believes that, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention (genus) commensurate to its scope at the time the application was filed.

SCOPE OF ENABLEMENT

Claims 45-52 and 55-85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a disorder of the respiratory system comprising administering a specific NF-kB decoy selected from the group consisting of SEQ ID NO:1 and 3, does not reasonably provide enablement for a method of **preventing** a disease of the respiratory system comprising administering **any NF-kB decoy** . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some 'experimentation.'" Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8

USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

SCOPE OF THE INVENTION

The breadth of the claims encompasses a method of **preventing a genus of diseases** of the respiratory system comprising administering any of **a genus of NF-kB decoys.** As discussed supra, the specification fails to describe the genus of NF-kB decoys and would require undue experimentation to discover these NF-kB decoys. Furthermore, the scope of the claims encompasses **preventing respiratory diseases** and there is no guidance for the breadth of such claims. The specification only discloses and provides guidance for a genus of NF-kB decoys selected from the group consisting of SEQ ID NO:1 and 3. Furthermore, the specification only provides guidance for treating a disorder of the respiratory system encompassed by the examples of the specification directed to animal models for asthma, rhinitis, and COPD.

GUIDANCE & WORKING EXAMPLES

The specification does not provide guidance for or a working example for **preventing** a respiratory disease. The working examples are directed to treatment with a composition comprising NK-kB decoys **after challenging** the animals with substances that induced symptoms of similar to those experienced by subjects suffering from asthma, rhinitis, or COPD. Therefore, there is no support for prophylactic treatment as encompassed by the breadth of the claims. The absence of working examples directed to pretreatment of subjects with NF-kB decoys prior to challenge or sensitization with inducers of asthma, rhinitis, and COPD symptoms necessitates further experimentation. In addition, none of the working examples utilize models which would mimic human respiratory diseases having an underlying genetic basis; framed another way, if the respiratory disease were genetically based, how could the disease be prevented? Additionally, no working examples were provided that utilize NF-kB decoys other than SEQ ID NO:1 and 3. Therefore, the specification does not provide sufficient guidance on how to make and use NF-kB decoys other SEQ ID NO:1 and 3 for treating conditions of the respiratory system due to expression of a gene regulated by NF-kB.

Furthermore, there are no examples of preventing diseases of the respiratory system. The scope of the claims is directed to the genus of diseases and conditions of the respiratory system due to expression of a gene regulated by NF-kB. NF-kB is involved in the regulation of numerous genes. The specification suggests some possible genes which might be involved in inflammatory diseases: "In the nucleus, NF-kB binds to an NF-kB binding site on a chromosome and promotes the transcription of a gene downstream thereof. A number of genes located downstream of NF-KB binding

sites, such as inflammatory cytokines (e.g., IL-1, IL-6, IL-8, tumor necrosis factor a (TNF a), etc.) and adhesion molecules (e.g., (e.g., VCAM-1, ICAM-1, etc.) are known." (page 6, lines 3-9). The only conditions cited in the specification as suitable for treatment with NF-kB decoys are: "airway inflammation, airway stenosis,...nasal cavity inflammation,...asthma,...nasal inflammation" (page 1, lines 19-23). The specification states, "COPD is initiated with normal symptoms, and gradually progresses, and thus is believe to be 'lung lifestyle-related disease'" (page 10, lines 18-20).

In addition, the Applicant does not disclose how the NF-kB decoys are to be used in order to prevent respiratory diseases. It is not clear from the specification, that in order for prevention of respiratory diseases, whether the patient is potentially prone for respiratory diseases or whether a recurrence is being prevented. Is the therapy to prevent recited here started months ahead or days ahead of a probable expectation of respiratory diseases? Is there a particular amount of the formulation that needs to be administered? Is a particular treatment regimen necessary? How long must such a treatment continue in order to prevent respiratory diseases? Further, Applicant has only shown that one of skill in the art would expect the incidence respiratory diseases to be reduced, not completely prevented. In view of the lack of guidance provided in the specification of the instant application, the level of unpredictability in the art in regards to methods of prevention and antisense/gene therapy, and the breadth of the given claims, it is concluded that undue experimentation would be required to practice the invention throughout the full scope of the claims, and therefore the invention is not enabled.

STATE OF THE ART & QUANTITY OF EXPERIMENTATION

In view of the state of the art and the level of the skilled in gene therapy art, it is still under development and highly unpredictable. *Orkin et al.* (NIH Report, 1995 Dec) reviews the infant state of the art of gene therapy from before the instant invention was made. The overall conclusions were: 1) gene therapy for each disease would present its own scientific and clinical challenges; 2) no successful gene therapy protocol was known; 3) significant problems remained in all aspects of gene therapy, especially with respect to effective expression vectors; 4) one cannot predictably extrapolate the result of one animal model, such as mouse, to treatment of a disease in a different animal, such as human; and 6) assessment of known gene therapy protocols was hindered by poor gene transfer, reliance on qualitative, rather than quantitative assessments of gene transfer, lack of suitable controls and poor definition of biochemical or disease endpoints (pages 1-2). Although the reference is ages old, the general status of gene therapy art has not significantly changed. *Peterson* (STATEMENT OF AMY PATTERSON M.D., February 2000) reviews "THE SUCCESS OF THIS TECHNOLOGY [GENE THERAPY] IS DEPENDENT UPON NOT ONLY THE DELIVERY OF GENETIC MATERIAL INTO THE TARGET CELLS, BUT ALSO THE EXPRESSION OF THE GENE ONCE IT REACHES ITS TARGET SITE. BOTH OF THESE REQUIREMENTS POSE CONSIDERABLE TECHNICAL CHALLENGES". *Peterson* further teaches that out of 372 clinical trials registered with the NIH, only one percent of the trials (3) have progressed to Phase III efficacy studies. "FOR THIS REASON, IT IS PERHAPS MORE ACCURATE TO REFER TO THIS TECHNOLOGY AS 'GENE TRANSFER', RATHER THAN 'GENE THERAPY', UNTIL THERE IS MORE EVIDENCE FOR THE THERAPEUTIC BENEFIT OF THIS TECHNOLOGY".

Specifically, gene therapeutic approaches to treat asthma are believed to be difficult, "evidence of the polygenomic nature of the disease and the inability to define a specific pathogenetic process linked to a final common pathway suggest that gene therapies probably will not be feasible, at least for the near future." (Leff. Chest 1997; 111:61S, abstract). In addition, Leff indicates several obstacles to a cure for Asthma in Table 1 (page 62S): (1) asthma is not a disease, (2) there is no single asthma gene, (3) the causes of asthma likely are varied, (4) different asthmas may require different therapies. Because of the difficulty in treating a NF-kB related disease such as asthma, the difficulty in preventing such a disease seems to be even more difficult.

CONCLUSION

In conclusion, given the breadth of the claims and the limited scope of the specification, an undue quantity of experimentation is require to make and use the invention beyond the scope of methods of treating a disorder and/or condition of the respiratory system due to expression of a gene regulated by NF-kB, comprising the step of administration of a composition comprising an NF-kB decoy selected from the group consisting of SEQ ID NO:1 and 3, and a pharmaceutically acceptable carrier to the respiratory system of a subject. The scope of the claims are **not enabled** for **preventing diseases** of the respiratory system due to expression of a gene regulated by NF-kB, comprising the step of administration of a composition comprising **any NF-kB decoy**.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 45-47, 52, 55 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated Lee et al. (FASEB Journal, 2001; 15:p.A663, #523.9 [provided in IDS filed 1/9/2006]). The prior art described below is applied o the extent that it discloses treatment of respiratory diseases due to expression of a gene regulated by NF-kB, comprising the step of administration of a composition comprising any NF-kB decoy.

Claim 45 is directed to a method for treating and/or preventing a disease, disorder and/or condition of the respiratory system due to expression of a gene regulated by NF-kB, comprising the step of: a) administration of a composition comprising an NF-kB decoy and a pharmaceutically acceptable carrier to the respiratory system of a subject. The specification teaches that a NF-kB decoy may be any oligonucleotide (page 24). Lee et al. teach administration of NF-kB p65 antisense oligonucleotide to an asthmatic mouse model, wherein treatment with the antisense oligonucleotide "resulted in significant inhibitions of airway eosinophilia...and improvement of airway hyperresponsiveness." Lee et al. further suggest, a "strategy to inhibit airway NF-kappa B activity may be beneficial to treatment of respiratory allergic diseases." The teachings of Lee et al. further satisfy the limitations of claims 46-47

(condition is airway inflammatory diseases, asthma). Although Lee et al. introduced the NF-kB decoy by intravenous injection, its activity has seen in the lungs, so the examiner interprets this as satisfying the limitation directed to administration to the respiratory system of the subject.

Claim 52 is directed to a method for treating and/or preventing a disease, disorder and/or condition of the respiratory system due to expression an eosinophil abnormality comprising the step of: a) administration of a composition comprising an NF-kB decoy and a pharmaceutically acceptable carrier to the respiratory system of a subject. The teachings of Lee et al. described above meet all the limitations of claim 52, particularly, treatment with the antisense oligonucleotide "resulted in significant inhibitions of airway eosinophilia."

Claim 55 is directed to a method according to claim 45, wherein said NF-kB decoy is a NF-kB decoy or a derivative, variant or fragment thereof, and the derivative, variant or fragment has a biological activity. Since claim 55 is not truly further limiting of claim 45 because it encompasses a broader scope (decoys and fragments), the teachings of Lee as described above, satisfy claim 55. Claim 59 has the same relation ship to claim 52 as claim 55 has to claim 45. Therefore, claim limitations of claim 59 are likewise satisfied by the teachings of Lee et al.

Accordingly, Lee et al. anticipated the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 45-52 and 55-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (FASEB Journal, 2001; 15:p.A663, #523.9 [provided in IDS filed 1/9/2006]) in view of Morishita et al. (US-6,262,033, issued 17 July 2001) and further in view of Debs et al. (US-5,641,662, issued 24 June 1997) and further in view of Cutie et al. (US-6,464,959, issued 15 October 2002). The prior art described below is applied o the extent that it discloses treatment of respiratory diseases due to expression of a gene regulated by NF-kB (particularly asthma, COPD, and rhinitis), comprising the step of administration of a composition comprising any NF-kB decoy.

Claim 45 is directed to a method for treating and/or preventing a disease, disorder and/or condition of the respiratory system due to expression of a gene regulated by NF-kB, comprising the step of: a) administration of a composition comprising an NF-kB decoy and a pharmaceutically acceptable carrier to the respiratory system of a subject.

Claim 52 is directed to a method for treating and/or preventing a disease, disorder and/or condition of the respiratory system due to expression an eosinophil abnormality comprising the step of: a) administration of a composition comprising an NF-kB decoy and a pharmaceutically acceptable carrier to the respiratory system of a subject.

Lee et al. teach administration of NF-kB p65 antisense oligonucleotide to an asthmatic mouse model, wherein treatment with the antisense oligonucleotide "resulted in significant inhibitions of airway eosinophilia...and improvement of airway hyperresponsiveness." Lee et al. further suggest, a "strategy to inhibit airway NF-kappa B activity may be beneficial to treatment of respiratory allergic diseases." The specification teaches that a NF-kB decoy may be any oligonucleotide (page 24). The teachings of Lee et al. further satisfy the limitations of claims 46-47 (condition is airway inflammatory diseases, asthma). Although Lee et al. introduced the NF-kB decoy by intravenous injection, its activity has seen in the lungs, so the examiner interprets this as satisfying the limitation directed to administration to the respiratory system of the subject. The teachings of Lee et al. described above meet all the limitations of claim 52.

Lee et al. do not teach the specific decoy, SEQ ID NO:1. Lee et al. also do not teach direct administration of the NF-kB decoy to the lung or nasal mucosa using a nebulizer, spray, respirator, or nasal drop. Lee et al. teach intravenous administration of NF-kB p65 antisense oligonucleotide.

Morishita et al. teach the specific NF-kB decoy, CCTTGAAGGGATTTCCCTCC, which is 100% identical to SEQ ID NO:1 of the instant application. This limitation is required in claims 56 and 60. Furthermore, Morishita et al. teach, "a method for treating NF-kB-associated diseases which comprises administering to an animal an effective amount of a polynucleotide NF-kB chromosomal binding decoy which antagonizes NF-kB mediated transcription of a gene located downstream of a NF-kB binding site where in said polynucleotide comprises..." CCTTGAAGGGATTTCCCTCC (col.7, lines 51-56). In addition, Morishita et al. indicate that asthma is one of the diseases that can be treated with the NF-kB decoy (col.1, line 16). Morishita et al. also teach a variety of pharmaceutical carriers and preparations, including liposomes, powders and liquid solutions (col.3, lines 1-6) [claims 50, 57, 58, 64] and stabilizers such as sucrose, lactose or starch, [claims 59 and 63-64] and also teach delivery in Sendai virus (col.3, line 17) [identified as HVJ-E envelope vector in claims 84-85].

Morishita et al. do not teach direct administration to the lung or nasal mucosa using a nebulizer, spray, respirator, or nasal drop.

Debs et al. teach, aerosol delivery of nucleic acids to cells of the airway and alveoli of the lung (abstract). Debs et al. describe nebulizers useful for airway delivery typical in the treatment of the airway inflammatory disease, asthma. [claims 48-52, 61-

62, 65-67, and 79]. Debs et al. also describe intranasal delivery (col.38, line 30). Debs et al. also describe delivery of 1mg/treatment to about 500 mg/treatment (col.21, line 55) [claims 76-77].

The Lee, Morishita and Debs references do not teach dry powder administration using metered dose inhaler (MDI) or dry powder inhaler (DPI) to treat asthma, COPD or rhinitis.

Cutie et al. teach, delivery of drugs (including nucleic acids) to the lung by way of inhalation for treating asthma and chronic obstructive pulmonary disease (col.1, lines 17-21) having aerosol particle sizes of less than 10 μm in diameter (col.1, lines 26-27) [claims 69-71 and 73-75] and can be administered using a metered dose inhaler (MDI) or dry powder inhaler (DPI) (col.1, lines 31-32) [claims 67-75]. Cutie et al. also teach a method of treatment by nasal inhalation (col.10, lines 23-27) [claims 78-79, 81-82] for treatment of rhinitis (col.8, line 46) [claims 80 and 83].

It would have been predictably obvious to the person of ordinary skill in the art at the time the invention was made to administer a particular NF-kB decoy, CCTTGAAGGGATTTCCCTCC, in a method for treating and/or preventing a disease, disorder and/or condition of the respiratory system using a nebulizer.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Each of the elements (treating asthma with NF-kB decoys, the particular NF-kB decoy (CCTTGAAGGGATTTCCCTCC), and using a nebulizer to administer agents to the lung for asthma treatments) are taught by Lee or Morishita or Debs or Cutie. In addition, methods of delivering nucleic acids using dry powder inhalation having micromolar diameter-sized particles were known in the art, as is illustrated by Cutie et al. It would be therefore predictably obvious to use a combination of these known elements in a treatment of asthma, rhinitis, and COPD with the particular NF-kB decoy, CCTTGAAGGGATTTCCCTCC.

Therefore the method as taught by Lee et al. in view of Morishita et al. and further in view of Debs et al. and further in view of Cutie et al. would have been *prima facie* obvious over the method of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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